Fowler (Geo. R.)

Two Cases of Rapidly Progressive Gangrene in which Pure Cultures of the Bacillus Pyocyaneus were found.

BY

GEO. RYERSON FOWLER, M. D.,

BROOKLYN,

Surgeon to St. Mary's Hospital and the Methodist Episcopal Hospital.

REPRINTED FROM

The New York Medical Journal

for February 10, 1894.

Reprinted from the New York Medical Journal
for February 10, 1894.

TWO CASES OF
RAPIDLY PROGRESSIVE GANGRENE
IN WHICH PURE CULTURES OF THE *BACILLUS PYOCYANEUS* WERE FOUND.

By GEORGE RYERSON FOWLER, M. D.,
BROOKLYN,
SURGEON TO ST. MARY'S HOSPITAL AND THE METHODIST EPISCOPAL HOSPITAL.

Case I.—J. B., aged thirty-one years, fishmonger. On November 18, 1892, I was requested by Dr. Curran to visit this patient in consultation. The following history was obtained: Two days previously, while cleaning fish, he received a wound from a fin upon the palmar surface of the distal phalanx of the left middle finger. The wound was a trifling one and attracted but slight attention at the time. Within a few hours, however, the finger became extremely painful and greatly swollen. The entire finger assumed a purplish-blue appearance, and several blebs filled with dark serum appeared upon the dorsal surface. When seen by me the local infection extended to the metacarpal region, and the finger itself was in a condition of gangrene from an overwhelmingly rapid infiltration of all its soft structures.

The patient's condition indicated a more than usually severe general infection. The pulse was 130 and the temperature 103° F. The countenance was anxious, the skin bathed in a moist, profuse perspiration, and in his general demeanor there were

the evidences of a profound disturbance of the nervous system, as shown by a general uneasiness, anxiety of countenance, and sleeplessness. The usual accompanying symptoms of the febrile state—namely, anorexia and furred tongue—were present.

Immediate operative interference, for the purpose of getting rid of the local source of infection, was advised and accepted, and he was removed to St. Mary's Hospital for that purpose. On the afternoon of the same day I amputated the finger, and removed at the same time the greater portion of the corresponding metacarpal bone and dissected freely away the gangrenous tissues upon the back of the hand.

Within a few hours the patient's temperature fell to normal, the pulse-rate lessened, and a general improvement followed. The wound, which had been dressed with moist compresses of Laplace's solution (mercuric chloride, 1 to 1,000; tartaric acid, 5 to 1,000), became and remained aseptic and rapidly healed by granulation.

Stab cultures of sterilized gelatin culture tubes were made of the contents of the blebs, and from the tissues of the finger, from which Dr. Bristow obtained, at the Hoagland Laboratory, pure cultures of the *Bacillus pyocyaneus* (Gessard).

Case II.—I. N., aged thirty-five years, was admitted to St. Mary's Hospital on January 5, 1892, suffering from an exceptionally severe attack of appendicitis. He had been attacked upon the preceding day with symptoms which indicated a more than usually severe and rapid form of the disease, as shown by the intensity of the local tenderness, as well as by the profound prostration and other grave constitutional symptoms. The abdomen was at once opened by a right lateral laparotomy. The appendix was found to be gangrenous from the tip to within a quarter of an inch of its base. It lay buried in a layer of plastic lymph, which, fortunately, had shut it off from the general cavity of the peritonæum. This layer of plastic lymph was of the same greenish black color as the appendix itself. Considerable difficulty was experienced in isolating and removing the appendix without disturbing the slightly adherent and thin layer of isolating new-formation tissue. In this, however, I was finally successful. The cavity from which the organ was re-

moved was carefully tamponed with sterilized zinc-oxide gauze, and the abdominal wound dressed with compresses of the same. All went well with the patient at first. The temperature and pulse-rate showed a decided tendency toward the normal from the first hour. The wound, as is my custom, was not disturbed for the first forty-eight hours. At the end of this time it was discovered that the patient's condition had changed for the worse. The temperature became elevated and the pulse quickened; some uneasiness on the part of the patient was also present. Upon removing the dressings, it was discovered that a gangrenous condition of the abdominal walls existed, extending from the inner margin of the wound toward the median line, occupying an area of about four inches. Numerous blebs were present, filled with dark-brown serum. The gangrenous portion was removed down to the muscular structure, which up to this time had escaped.

The parts were thoroughly cleansed by means of the acid-sublimate solution, and both the cavity from which the appendix was removed as well as the infected abdominal wall were dressed with moist dressings of the same. These were frequently changed. The wound soon assumed a healthy appearance, the pulse and temperature fell rapidly to the normal, and the patient eventually made a complete and satisfactory recovery.

Stab inoculations in culture tubes of sterilized gelatin, derived both from the contents of the blebs and from the gangrenous tissue, were made and investigated, with the result of showing the presence of the *Bacillus pyocyaneus*. No other micro-organism was found.

The special interest to be attached to these cases depends upon the bacteriological findings, taken in connection with the clinical conditions present. In both the same phenomena of sudden and rapid supervention of grave constitutional symptoms, in conjunction with a rapidly progressive gangrenous local condition, marked the course of the case. In both the same rapid improvement followed removal of the gangrenous area and vigorous antibacterial

local treatment. Finally, in both the same micro organism, and that of the class to which but slight pathogenetic importance is usually attached, was found in pure culture.

The question of the pathogenetic importance of this bacillus is of considerable interest at the present time. Former observers have considered its presence of but slight moment, producing no injurious effect; on the contrary, some have considered the occurrence of bluish-green pus as a favorable omen, inasmuch as gangrene and septic complications were usually not observed in connection with green suppuration. Since the days when "good and laudable" pus was considered a good omen in the course of the healing process, green or blue pus has lost its fascination for the surgeon, particularly since recent experiments (Lederhose, Bouchard) have shown, as already stated, that, in animals destitute of immunity (guinea pigs and rabbits), subcutaneous or intraperitoneal injections of recent cultures in bouillon caused the death of the animal in from twelve to thirty-six hours. In the case of the subcutaneous connective tissue an extensive inflammatory œdema and purulent infiltration of the tissue spaces, and in the case of the intraperitoneal injections a sero fibrinous or purulent peritonitis, is induced. The cultures can be recovered from the serum or purulent fluid in both localities, as well as from the blood and the various organs. These results follow the introduction of one cubic centimetre or more of the bouillon culture. The introduction of smaller quantities may only be followed by local disturbances (abscesses), but thereafter the animal becomes immune against the usual toxic dose for animals of its class. Immunity may also be brought about by the introduction of the toxic products of the bacillus in bouillon, the latter being sterilized.

An antagonism between this micro organism and the bacillus of anthrax has been supposed to exist from the

fact that animals inoculated with the latter are found to recover after inoculation with a pure culture of the *Bacillus pyocyaneus* (Bouchard, Charrin, and Guignard). This is probably due to the antidotal effects of the chemical products resulting from the proliferation of the bacillus (Woodhead and Wood), as shown by the fact that the same effect was produced if a sterilized culture of the saprophyte is introduced following the anthrax infection.*

Injections of cultures of Gessard's bacillus into the veins of animals produced the most pronounced toxic symptoms. From forty-five to sixty cubic centimetres of a culture, from two to three days old, introduced into the jugular vein of a dog produced death of the latter with characteristic symptoms, consisting of high fever, vomiting, and dejections of bloody fluid. Upon the death of the animal, section disclosed extensive hæmorrhagic and inflammatory conditions of the intestinal tract, together with subendocardial blood extravasations (Bergmann). Intravenous injections into the auricular veins of rabbits invariably produced death, even in relatively small doses (Charrin). Doses insufficient in amount to produce death usually induced paralysis in the posterior extremities, and albuminuria, the result of renal changes. In lethal cases a more acute course followed, characterized by fever, diarrhœa, and albuminuria. Intravenous injections are most pronounced in their effects; next comes subcutaneous and intraperitoneal inoculations. Exposure of the air-passages and of the intact gastro-intestinal mucous membrane to the action of the bacillus gave negative results.

Varying degrees of immunity and susceptibility are observed in different animals and in individual specimens of the same animal. For instance, some rabbits will rapidly perish from the usual toxic dose, while others remain alive

* Sternberg. *Manual of Bacteriology.*

after a much larger dose. Still others appear unaffected at first, but die after weeks or months of apparent health.

The later experiments of Bergmann would seem to show that neither progressive phlegmon nor sepsis occur with minimal doses of the culture of the *Bacillus pyocyaneus.* Even the most virulent cultures applied to open wounds have apparently but little effect. The effect in larger quantities, however, seems to be in direct proportion to the dosage. Even with larger doses of the bouillon cultures injected subcutaneously, while local abscesses and general toxic effects manifest themselves, the occurrence of progressive suppurative processes or of pyæmic metastases to remotely placed articulations, or to the internal organs, are not observed. In the cases in which abscesses are produced by subcutaneous injection of the bacillus the latter can be identified in the pus for a considerable time afterward and cultures made therefrom. The micro organism, however, can not be identified in the surrounding tissues, nor does it appear to enter the circulation of the blood. When intravenous injections are employed, however, particularly in conjunction with an emulsion of sterilized lard, suppurative infarction in the lungs takes place. In addition to this, larger injections into the jugular veins of rabbits are followed, even in those instances in which rapid death occurs by the presence of the micro organism in all of the internal organs and in the blood as well. If, however, injections which are insufficient to produce death are given in a number of animals, and these killed at varying periods of time, it will be found that the bacillus will disappear, first from the arterial circulation, next from the lung tissue, following this from the liver and spleen, and last of all from the kidneys. They are found in large numbers in the urine and bile, thus suggesting that the liver and kidneys act as eliminators of the bacilli. This progressive

elimination of the micro organism would seem to prove that no proliferation, but rather a decrease in the number of the bacilli, takes place. This occurs partly by destruction in the fluids of the body and partly by elimination through the organs above mentioned.

It would therefore appear that the picture presented of the behavior of animals under the influence of this saprophyte suggests rather an intoxication, either local or general, than symptoms resulting from an area mycosis. The fact that the effect is increased or diminished in proportion to the dosage, and the absence of advancing symptoms as well as evidences of proliferation of the bacillus in the tissues, recall the influence of irritating chemical agents upon the animal rather than the gradually progressive processes of disease based upon the advance of bacteria. This is further increased by the fact that the toxic products of the disease in bouillon cultures of the bacillus are not destroyed, although somewhat diminished by repeated attempts at sterilizing by heat at the boiling point. The removal of all corpuscular elements by filtration is equally inefficient with heat in eliminating the poisonous bacterial proteines, as Binhuer calls the albuminous portions of the bacterial cells which this observer located in the latter, and upon which the effects of the bacillus, notably the high temperature and inflammation, depend. It seems to be definitely settled that the toxic properties do not reside in the pyocyanin or the pigments generally, for the reason that even in large doses these are quite harmless. On the other hand, the bacterial proteins—which are obtained by scraping cultures grown upon a solid pabulum, such as potatoes, and dissolving these in weak alkaline solutions—are capable of producing the symptoms, even after heat sterilization and filtration, usually attributed to the presence of the bacillus in living cultures.

The fact should not be lost sight of, in considering the question of the toxic influence of cultures derived from the *Bacillus pyocyaneus*, that these are not conditions specifically related to or characteristic of this micro-organism. These symptoms of local irritation and general intoxication are common effects of bacterial infection from many sources.

There are numerous recorded observations of the presence of the *Bacillus pyocyaneus* under circumstances which would seem to suggest, with some degree of plausibility at least, that this micro-organism bore some ætiological relation to the conditions present. Thus it has been found in the pus from a suppurating otitis media (Gruber). It has been observed in septic peritonitis together with the *Bacillus communis* and other micro-organisms. It was found post mortem in the hepatized lung of a child an hour and a half after death in conjunction with the *Proteus vulgaris* (Neumann). In a case which simulated typhus an eruption of bullæ occurred in the inguinal region in the third week. The blebs filled with a bluish serum, from which pure cultures of the *Bacillus pyocyaneus* were obtained (Oettinger). A rather interesting observation is made by Ehlers: Two children fell sick with diarrhœa, fever, albuminuria, and symptoms suggestive of typhus or cerebro spinal meningitis. In one case an eruption of blebs occurred on the twelfth day, the contents of which were bluish in color. Pure cultures of the *Bacillus pyocyaneus* were obtained from these. In the other case pure cultures of the same organism were obtained from the blood post mortem. While at first sight some of these cases seem striking, yet it must be admitted that they are scarcely convincing. The ætiological relations between the bacillus found and the conditions present in any given case is always a difficult matter to establish. For instance,

the natural habitat of the bacillus has been shown to be the skin of the patient himself.* Green suppuration occurs with especial frequency about the axillary cavity, the gluteal furrow, and the inguinal fold (Muchsam). Eberth's researches have shown that the greenish-blue color imparted to the underclothing of some individuals depends upon the proliferation of this bacillus. It is a matter of common observation that the portions of the garments which come in contact with these localities are the site of these discolorations. This would explain the occurrence of the organism in the blebs in the inguinal region in Oettinger's case, in those following burns, and, in fact, in all the cases in which it has been found upon the integumentary surface. The fact that this organism is found in pure culture does not necessarily prove in any case that it was the true pathogenetic agent, for the latter may have easily escaped detection because of errors of inoculation, the absence of a proper culture media, etc. Gruber's observation is likewise open to criticism, for the tenacity of the *Bacillus pyocyaneus* when suspended in pus is well known, while the readiness with which certain other bacteria are inhibited in their growth or destroyed altogether by the presence of phagocytes should be borne in mind.

In considering the cases in which certain phenomena of

* The origin of the bacillus of green or blue pus has recently become a subject of considerable interest to the surgeon. De Symmes investigated the condition of the atmospheric air in the operating room of Bergmann's clinic, and in several hundred plates and more than four thousand varieties of micro-organisms this bacillus was identified in but one instance. And this occurred at a time when a large number of cases of green suppuration were being dressed in the clinic. The constant employment of dressing materials made rigidly aseptic by exposure to heat above the thermal death point of the bacillus renders it very improbable that they convey the germ, since it is found to occur when such dressings are employed.

a general character are recorded as having occurred in connection with the organism under consideration, several facts should be borne in mind. First the frequent occurrence of the bacillus upon the skin and presence of blue or green pus under circumstances of entirely undisturbed general health of the individual. Of the large number of cases of blue or green suppuration seen at the various clinics in the course of a year, I have yet to hear of a well-authenticated instance in which the nervous and febrile phenomena observed in both of the cases here recorded occurred. As to the discovery of the bacillus in the blood and internal organs post-mortem, this may be explained by the facility and rapidity with which saprophytic bacteria of both the skin and intestinal canal invade the tissues after death.

While, therefore, it is comparatively easy to account for the presence of the *Bacillus pyocyaneus* in the pus of middle-ear disease, in the blebs or blisters the result of burns, as well as those which occur as exanthemata, and in the blood and internal organs of those dying from symptoms resembling typhus and cerebro-spinal meningitis, and from which presence a pathogenic significance has been drawn, in all probability without due weight being given to all of the factors entering into the cases as they occurred, and the observations as they were made, it is difficult to explain the presence of the micro-organism in pure culture in the tissues of living patients, as occurred in the cases the histories of which have been given, without attributing to them a pathogenetic significance.

The possibility of some other micro-organism being mistaken for the one under discussion is, of course, always among the possibilities. Or, like the *Bacillus coli communis*, it may be that under certain circumstances the *Bacillus pyocyaneus* may assume pathogenetic properties in man not usually attributed to it.

In this connection the observations of H. C. Ernst are of interest. This writer discovered a bacillus in the fluid taken from a case of pericarditis which resembled that of blue or green pus in some respects, but which differed from the latter, as claimed by Ernst, in several important particulars. He claims that the micro-organism, which he identified and which he has called the *Bacillus pyocyaneus pericarditidis*, is a distinct variety of the bacillus of Gessard, and that therefore the assertion of the latter that there is but one blue-pus bacillus is unfounded.* The pathogenesis of H. C. Ernst's bacillus appears to be essentially the same as that usually attributed to the bacillus of Gessard, save that a somewhat smaller dose suffices to produce the effect.

To sum up, therefore, it may be stated: 1. That the destructive and profoundly toxic effects which characterize the presence of the *Bacillus pyocyaneus* in the lower animals have not heretofore been observed to occur in man. 2. That where its presence has been discovered in connection with pathological conditions the pathogenetic significance of the organism has not been established, for the reason that heretofore there has not been placed upon record a single well-authenticated case in which the *Bacillus pyocyaneus* was present in pure culture in the living tissues of the patients. Its presence in the blebs of Oettinger's case of typhus offers no more significance than is offered in those cases in which it is found in the blebs following burns. 3. The utmost that any of the observers who have studied this organism have yet claimed is that it delays the healing process, particularly the formation of new integumentary covering to the granulations, and produces a slow, chronic, but not intense toxæmia.†

* Ernst. Bacillus Pyocyaneus Pericarditidis. *American Journal of the Medical Sciences*, October, 1893.

† Schimmelbusch. *Sammlung klinischer Vorträge*, No. 62.

Viewed from this standpoint, the observations herewith recorded may be looked upon as somewhat unique, suggesting, at least, that although this organism has no special tendency to invade the living tissues, yet that, under certain yet unexplained conditions of growth or environment, they may become thus migratory and give rise, unless promptly followed up, to the most disastrous consequences. Or a bacillus similar to that of Gessard, as well as that claimed by H. C. Ernst, not distinguishable by means now at our command from that of green or blue pus, but possessing a pathogenic importance not attributable to the latter, may have been the noxious and infective agent at work in these cases.

The truth of the matter will probably be found in the statement that the world is but upon the threshold of bacteriological science, and that most remarkable revelations are yet to come. The cases herewith presented are offered with the hope of stimulating research and possibly identifying a special organism bearing an ætiological relation to cases of rapidly progressive gangrene.